Synthesis of an arrayed sgRNA library targeting the human genome

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Supplementary Material

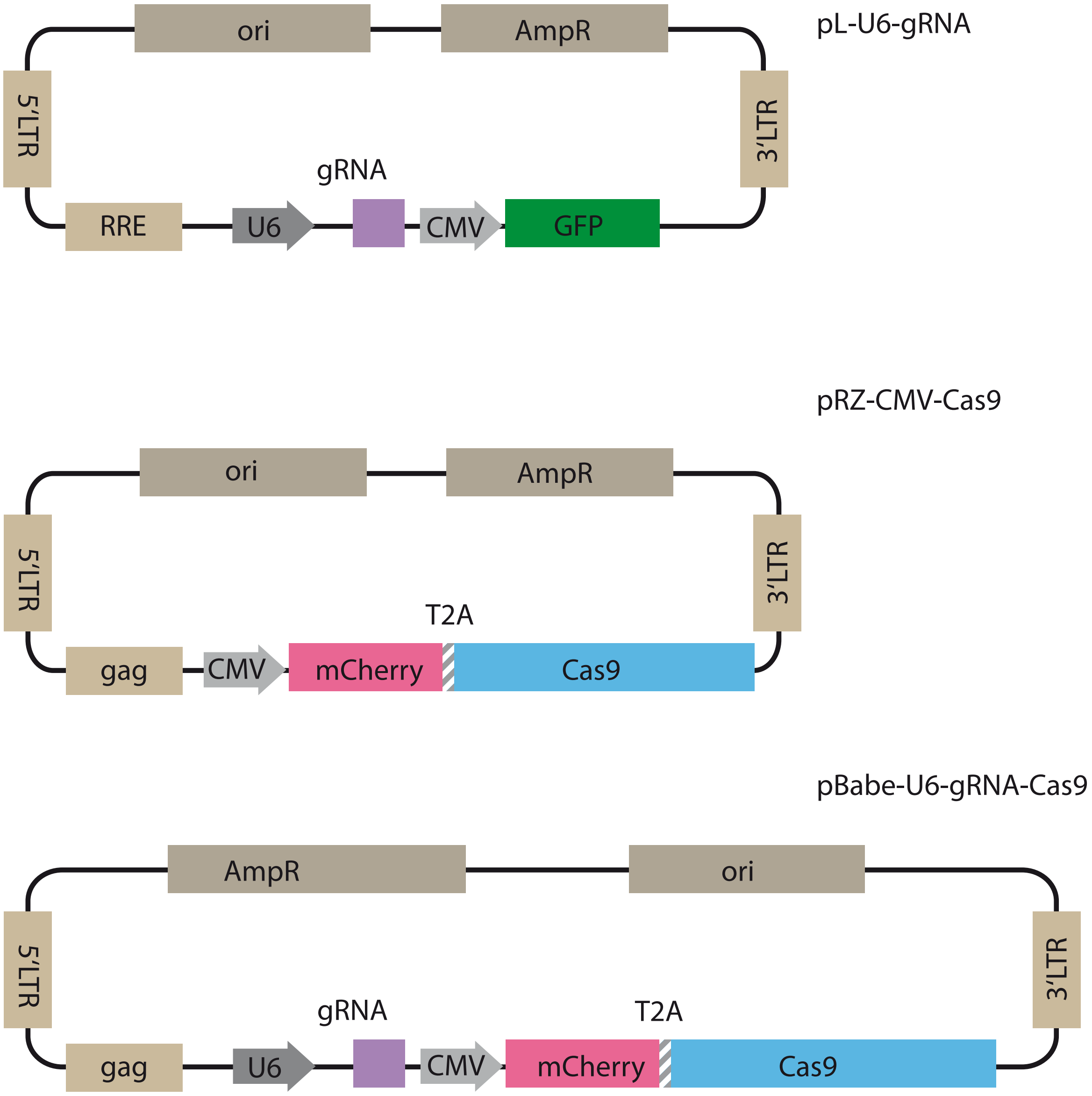
Supplementary Figures 1-8

Supplementary Notes

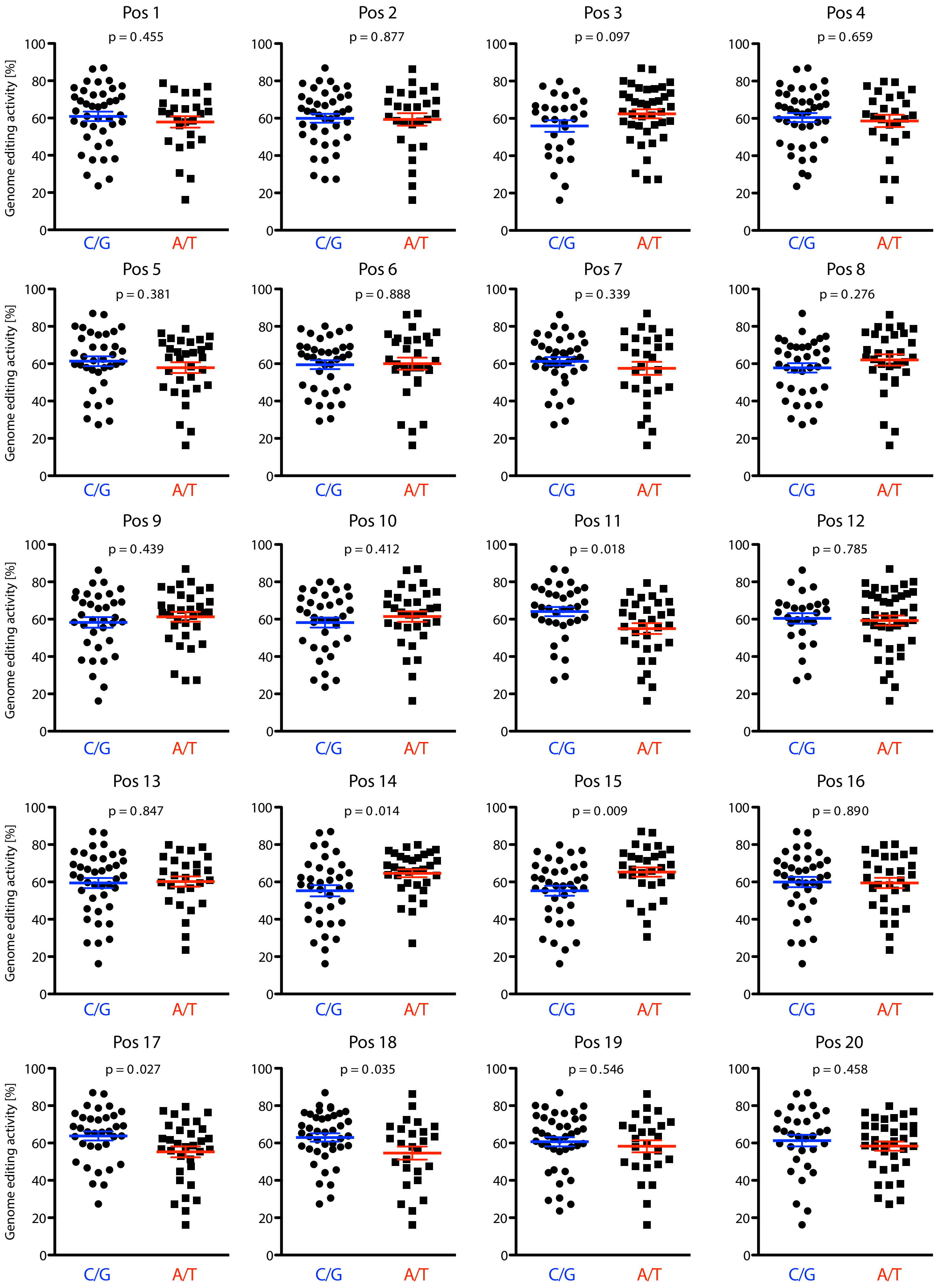
Supplementary Methods

Supplementary Tables 1, 2, 5, 6 and 7

Supplementary Tables 3 and 4 (see additional XLS spreadsheets)



Supplementary Figure S1 | CRISPR/Cas9 Vectors. Depicted are three different vector: pL-U6-gRNA contains a LIC ready sgRNA cassette driven by a U6 promoter, followed by a CMV promoter-driven GFP cassette. pRZ-CMV-Cas9 contains an mCHerry-Cas9 cassette that is seperate by a T2A peptide and driben by a CMV promoter. pBABE-U6-gRNA-Cas9 contains both a LIC ready sgRNA cassette driven by a u6 promoter and a mCherry-Cas9 cassette that is seperated by a T2A peptide and is under control of a CMV promoter. pL-U6-gRNA additionally contains lentiviral packaging elements while pRZ-CMV-Cas9 and pBabe-U6-gRNA-Cas9 contain retroviral packaging elements.



Supplementary Figure S2 | Base pair composition of the target site. Shown is the genome editing activity of the 67 sgRNA constructs depicted in Figure 2 as a function of their C/G or A/T content at position 1 to 20 (N of NGG in the PAM is position 21). Mean ± SEM is highlighted in colors (G/C blue, A/T red). Statistical analysis was performed using a two-sided, unpaired t-test, whereas nominal p values are depicted.

1.) Fetch all annotated mRNAs (NCBI RefSeq).

↓

2.) Identify longest open reading frame (ORF)

- If an in-frame *ATG* is present within the first 80 bases of an ORF: shift ORF boundary to that *ATG*.
- Select the first half of the ORF for target site identification.

↓

3.) Generate list of suitable spacer/protospacer regions (5′-N$_{21}$GG-3‘ or 5‘-CCN$_{21}$-3‘)

- must map to genome (UCSC hg19 assembly).

↓

4.) Calculate activity score based on targeting algorithm:

- A or T at position 14 = score +1
- A ot T at position 15 = score +1
- G or C at position 18 = score +1
- if GC content in region 2 ... 20 < 35%: set score = 0

↓

5.) Determine number of target sites of the PAM-adjacent 13-mer sequence within genome.

↓

6.) Pick spacer/protospacer region according to the following priorities (list 1 - 4):

activity score = 3 or 2

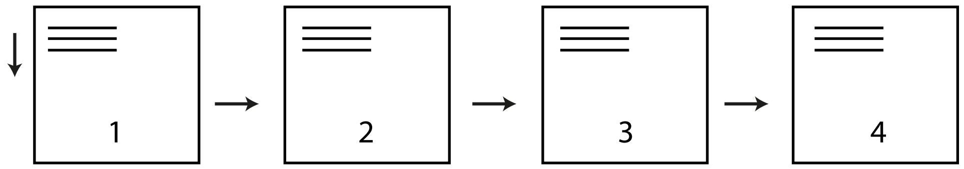
activity score = 1 or 0

target sites = 1

target sites = 2

target sites = 1

target sites = 2



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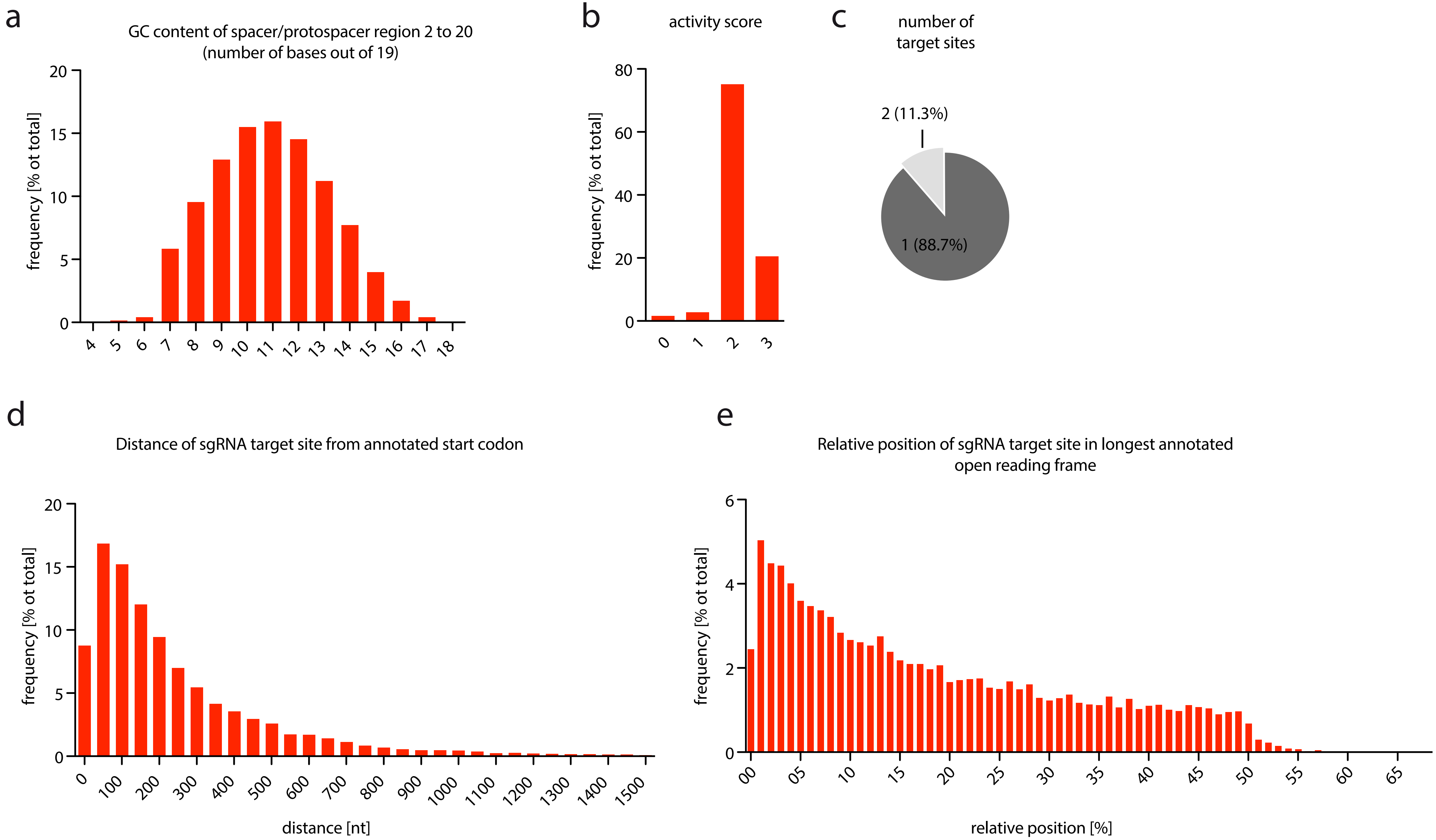
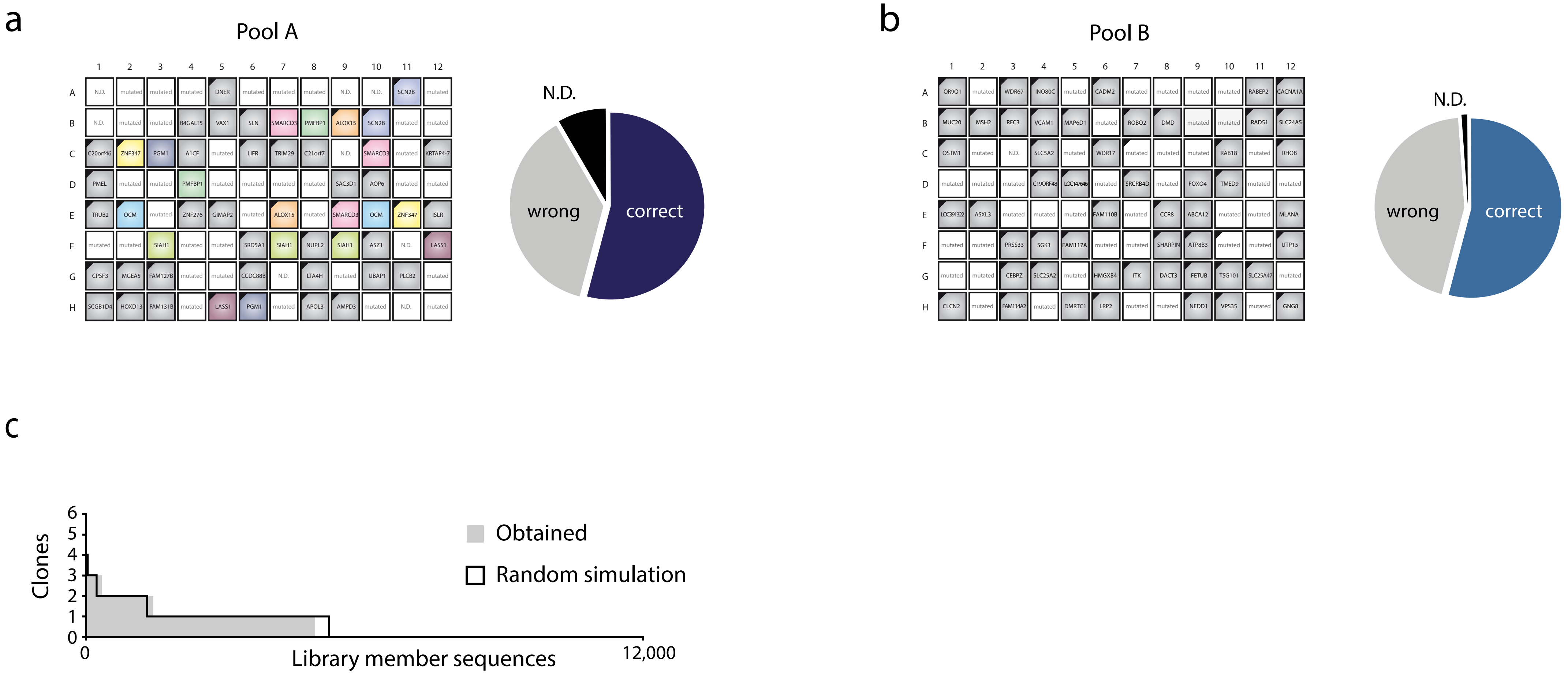
7.) Eliminate duplicate spacer/protospacer regions from total pool.

Supplementary Figure S3 | Description of the sgRNA^{KOLIBRY} library design. A detailed workflow of the algorithm for the design of a genome-wide human CRISPR library sgRNA^{KOLIBRY} is depicted (please see Supplementary Note 2 for details).



Supplementary Figure S4 | Design characterisitics of the sgRNA^{KOLIBRY} library. Depicted are histograms that show (**a**) the GC distribution, (**b**) the activity score according to the library design algorithm and (**c**) the pie chart shows the proportion of sgRNAs with one or two target sites of the PAM-adjacent 13-mer region. (**d** and **e**) Histograms depict the absolute (bin width 50 nt) and relative distance (bin width 1%) of the sgRNA target site from the start codon. Note that target sites beyond 50% of the ORF are obtained due to the fact that an offset of 80 nt from the first start codon is considered for some targets.



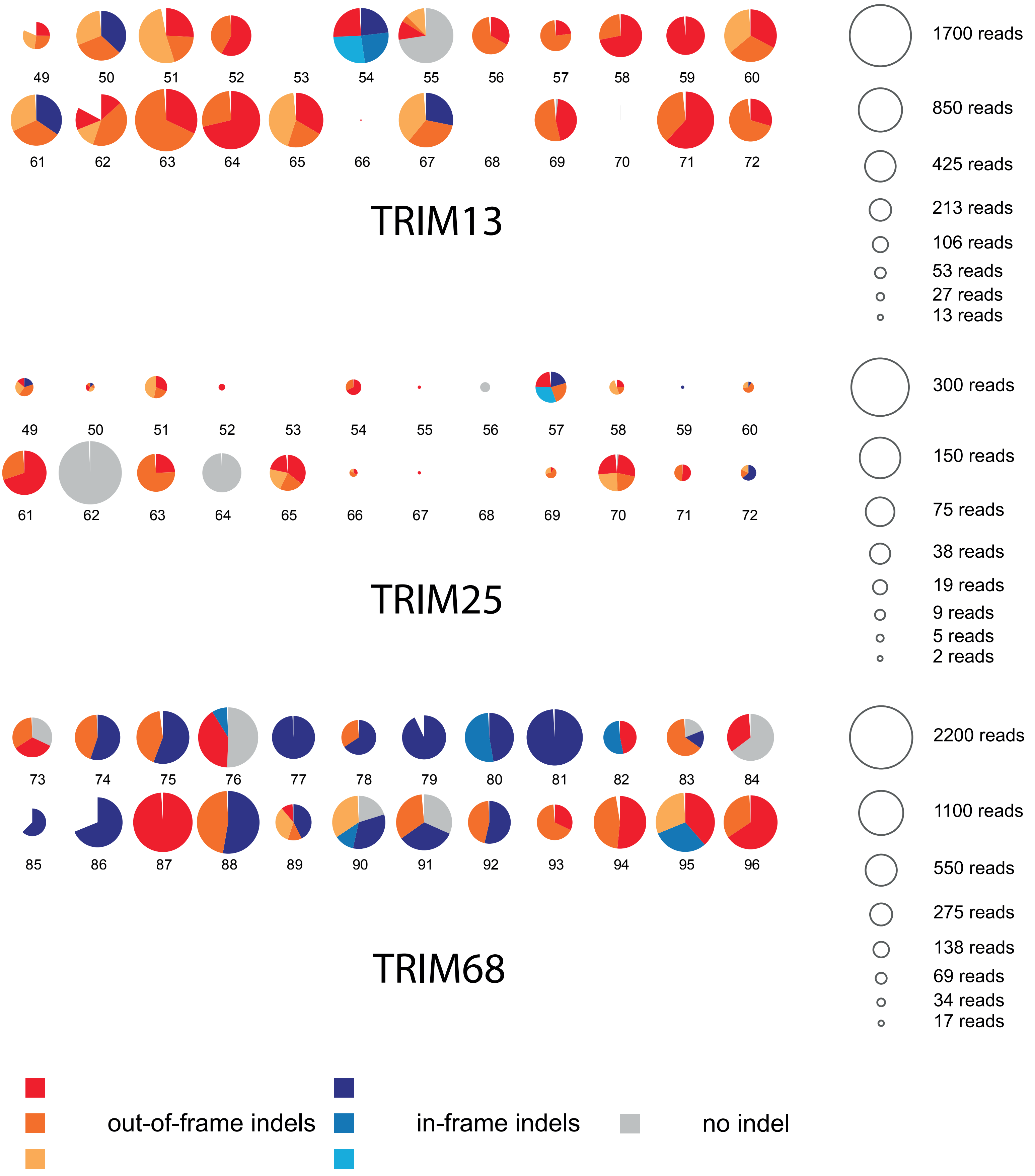
Pool A

	1	2	3	4	5	6	7	8	9	10	11	12
A	N.D.	mutated	mutated	mutated	DNER	mutated	mutated	mutated	N.D.	N.D.	SCN2B	mutated
B	N.D.	mutated	mutated	B4GALT5	VAX1	SLN	SMARCD3	PMFBP1	ALOX15	SCN2B	mutated	mutated
C	C20orf46	ZNF347	PGM1	A1CF	mutated	LIFR	TRIM29	C21orf7	N.D.	SMARCD3	mutated	KRTAP4-7
D	PMEL	mutated	mutated	PMFBP1	mutated	mutated	mutated	mutated	SAC3D1	AQP6	mutated	mutated
E	TRUB2	OCM	mutated	ZNF276	GIMAP2	mutated	ALOX15	mutated	SMARCD3	OCM	ZNF347	ISLR
F	mutated	mutated	SIAH1	mutated	mutated	SRD5A1	SIAH1	NUPL2	SIAH1	ASZ1	N.D.	LASS1
G	CPSF3	MGEA5	FAM127B	mutated	mutated	CCDC88B	N.D.	LTA4H	mutated	UBAP1	PLCB2	mutated
H	SCGB1D4	HOXD13	FAM131B	mutated	LASS1	PGM1	mutated	APOL3	AMPD3	mutated	N.D.	mutated

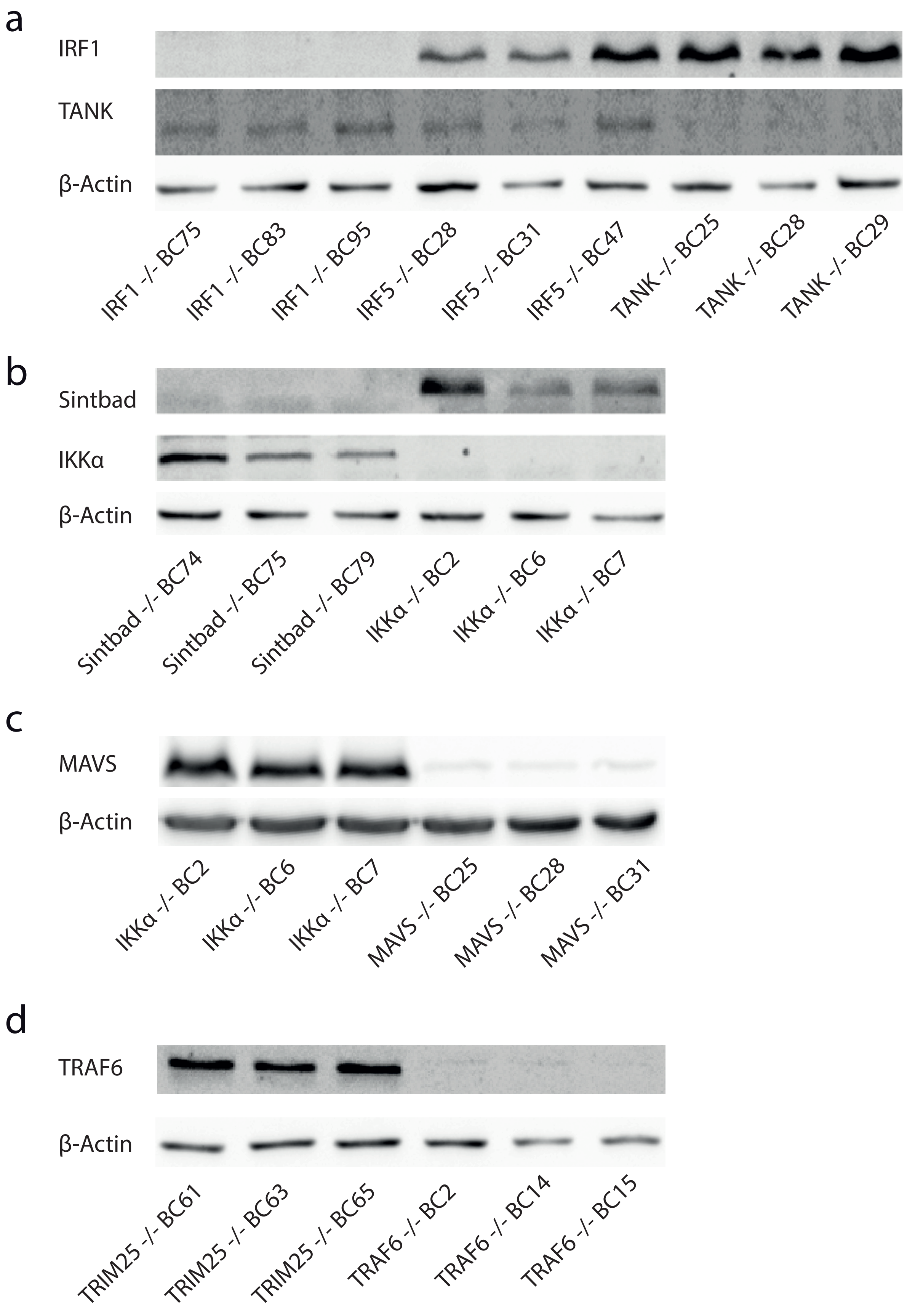
Pool B

	1	2	3	4	5	6	7	8	9	10	11	12
A	QR9Q1	mutated	WDR67	INO80C	mutated	CADM2	mutated	mutated	mutated	mutated	RABEP2	CACNA1A
B	MUC20	MSH2	RFC3	VCAM1	MAP6D1	mutated	ROBO2	DMD	mutated	mutated	RAD51	SLC24A5
C	OSTM1	mutated	N.D.	SLC5A2	mutated	WDR17	mutated	mutated	mutated	RAB18	mutated	RHOB
D	mutated	mutated	mutated	C19ORF48	LOC147646	mutated	SRCRB4D	mutated	FOXO4	TMED9	mutated	mutated
E	LOC391322	ASXL3	mutated	mutated	mutated	FAM110B	mutated	CCR8	ABCA12	mutated	mutated	MLANA
F	mutated	mutated	PRSS33	SGK1	FAM117A	mutated	mutated	SHARPIN	ATP8B3	mutated	mutated	UTP15
G	mutated	mutated	CEBPZ	SLC25A2	mutated	HMGXB4	ITK	DACT3	FETUB	TSG101	SLC25A47	mutated
H	CLCN2	mutated	FAM114A2	mutated	DMRTC1	LRP2	mutated	mutated	NEDD1	VPS35	mutated	GNG8

Supplementary Figure S5 | Elimination of clone duplicates validated by individual sequencing of sgRNAs from two individual pools. Sequencing results from 96 representative sgRNA library clones picked from pool A (**a**) or pool B (**b**). Indicated are the identifiers of the genes targeted by the retrieved correct sgRNA sequences, mutated sgRNA sequences (mutated), and plasmids that could not be sequenced (N.D.). Colors highlight sgRNA sequences that were observed more than once on the same plate. Black triangles in a well indicate that the respective clone was also identified by orthogonal mixing. Pie chart summarizing the identified sgRNA oligos that are depicted in (**c**). The coverage of individual library members picked from pool B is depicted as compared to a simulation assuming a complete random distribution of library members with no sequence or founder bias.

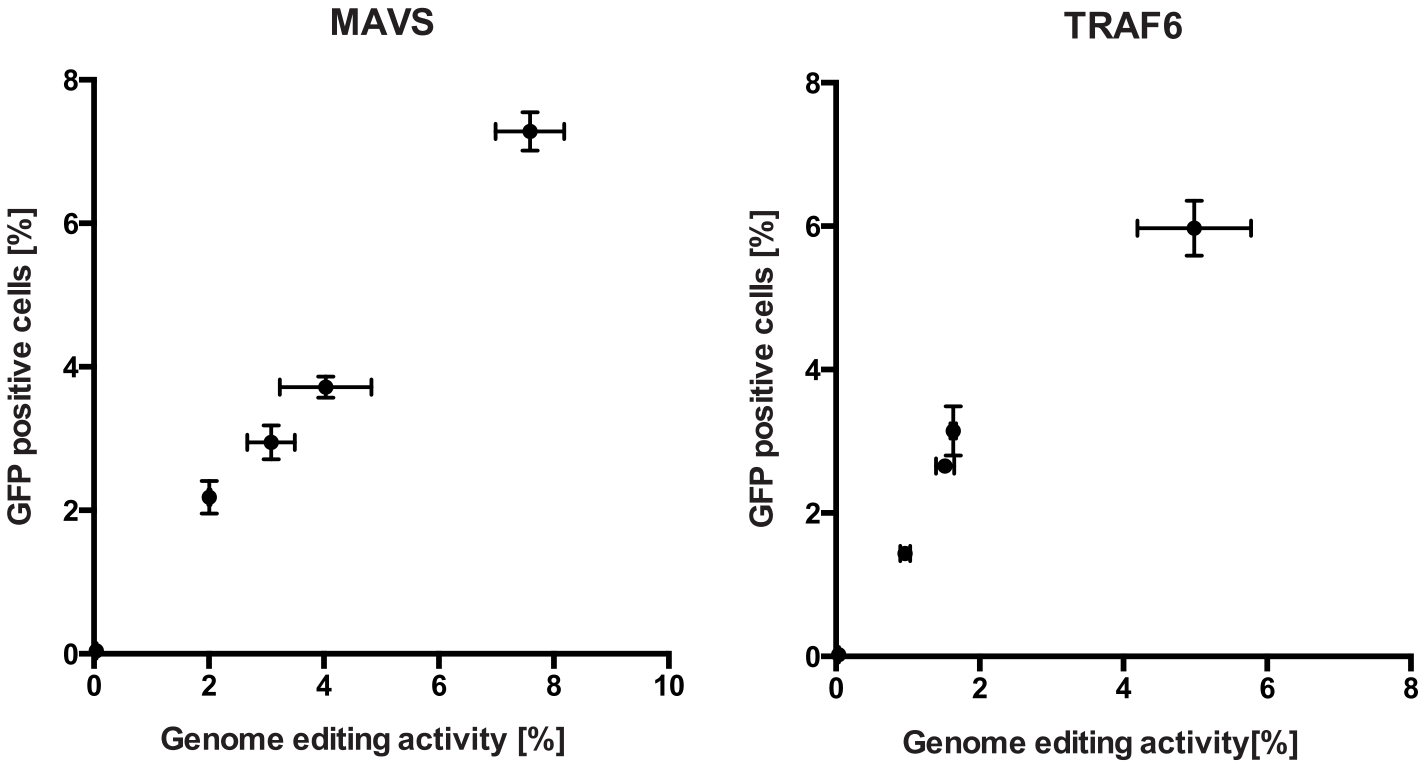


Supplementary Figure S6 | OutKnocker analysis of 19 individual gene targeting projects. Depicted is the deep sequencing result of 19 gene targeting projects analyzed by the web tool OutKnocker. For every gene targeting project 24 clones were picked and sequenced. Each pie pieces sums up all reads that have the same mutation and represents the proportion of total reads analyzed. Grey pie charts show reads without indel mutations, blue colors indel mutations that are in frame, whereas red colors indicate indel mutation reads that are out of frame.



Supplementary Figure S7 | Expression analysis of six different target genes by immunoblot. Lysates of knockout cell clones were probed for β-Actin, (**a**) IRF1 and TANK, (**b**) Sintbad and IKKα, (**c**) MAVS or (**d**) TRAF6. Knockout cell clones with different genotypes served as wildtype controls. The genotype is indicated on the bottom of the blots, BC indicates the barcode combination that was used for deep sequencing to identify individual clones.

Correlation between transduction efficiency and genome editing activity



Supplementary Figure S8 | Correlation between transduction efficiency and genome editing activity. HEK 293T cells stably expressing Cas9 were transduced with different amounts of lentivirus containing a library plasmid expressing the sgRNA for MAVS and TRAF6. Depicted are plots that show the correlation between the transduction efficiency of the lentiviruses and the genome editing activity in HEK293T cells. Shown are mean values of three independent replicates +/-SEM.

Supplementary Notes

Orthogonal mixing and clone calling considerations

The orthogonal mixing strategy we applied allows allocating library member sequences within a large number of library clones while requiring a significantly lower number of PCR reactions and barcoding primer combinations in comparison to the number of clones to be analyzed (Figure 3).

Considering one set of 32 clone plates, an exemplary library sequence found only in position A1 of the respective position-based mixing plate and only in pool I on the group-based mixing plate can be clearly allocated to position A1 on plate 1 of the set. However, when considering a library sequence present twice within a set of 32 clone plates, it depends on the localization of the duplicates if the position of both clones can be unambiguously recovered from the data. For example, if the duplicates are located on a single plate of the set at two different positions, a reliable call is possible. However, considering a library sequence present on plate 1 at position A1 as well as on plate 2 at position A2, the respective sequence would appear twice in the set of the position-based mix plates and twice in the set of the group-based mix plates. As such, it is impossible to conclude from the sequencing data if the sequence is located at (plate 1 A1) and (plate 2 A2) or, alternatively, at (plate 1 A2) and (plate 2 A1). Therefore, any clone calling algorithm must reject calling these positions. Consequently, sequence duplicates do not only reduce the coverage of a library by reducing the total number of individual clones being picked, but also do so by reducing the number of unambiguously allocatable sequences if the duplicates appear within qualifying relative locations among the clone plates.

In the clone library picked from pool A, we observed a high number of clonal duplicates among 96 clones picked from a single transformation reaction streaked on a single agar plate. This is in line with our observation that after 29,568 picks out of a library of 19,956 member sequences at a per-clone fidelity of 54.2%, only 39.4% of library sequences were recovered, while a random clone picking simulation predicts 55.2% of the library to be covered according to the equation:

$$\textit{Expected Coverage} = 1 - ((1-(1/\textit{Library Sequences}))\ \hat{}\ (\textit{Pick Number} * \textit{Fidelity}))$$

A likely explanation for the obvious phenomenon of clonal duplicates within clone sets or on single clone picking plates is that during recovery from transformation before agar plate streaking, bacterial clones might have divided one or two times. Indeed, when we omitted the 1 h recovery step prior to plating the transformed bacteria (pool B), a much lower number of clonal duplicates was observed.

The sgRNA$^{\text{KOLIBRY}}$ target site selection criteria

After extracting a list of all annotated human mRNA sequences from the current NCBI Reference Sequence Database, every mRNA sequence was scanned for start codons by the sequence *ATG*. At every start codon, the length of a possible open reading frame (ORF) was determined by seeking the first cognate stop codon with the sequence *TGA*, *TAG* or *TAA* shifted downstream by 3 x n bases. Of all ORFs identified in a given mRNA, only the longest ORF was considered for further analyses. To rule out the possibility that an alternative, cognate start codon in the same reading frame renders CRISPR targeting inefficient for disrupting functional gene expression, the first 80 bases of the longest identified ORF were scanned for the presence of secondary in-frame start codons. Upon encounter of such, the

ORF boundary was shifted to that additional, upstream *ATG*. Next, possible CRISPR target sites were identified by searching the sequence 5’-N_{21}-GG-3’ or 5’-CC-N_{21}-3’ with the limitation that the target site has to match the human genome (UCSC hg19 assembly). To avoid the possibility of expressing truncated proteins that still retain the full or partial functions of the full-length protein, only target sites located within the first half of the ORF were considered. This measure also increases the likelihood of subjecting the frame-shifted mRNA molecule to nonsense mediated mRNA decay. For all chosen target sites an activity prediction score was calculated based on the base preferences at position 14, 15 (A or T) and 18 (C or G) we observed. We focused on these three positions for their location in the PAM-proximal seed region and as a trade-off between enhancing sgRNA activity and limiting the possible targeting space. Previous studies had identified that point mutations within the PAM-proximal seed region of 6-13bp strongly impact on DNA cleavage activity by the CRISPR:Cas9 complex. Therefore, to limit off-target effects, we favored target sites for which the PAM-proximal 13bp sequence was most unique in the human genome. Considering these criteria, target sites were identified in a hierarchical selection process as depicted in Supplementary Figure 3. The best target site per target gene was then chosen for the genome-wide sgRNA library, whereas the characteristics of these target sites are depicted in Supplementary Figure 4.

Supplementary Methods

CRISPR sgRNA assembly

Backbone preparation

10 µl of the sgRNA entry vector (200 ng/µL in H_2O) were digested with ApaI and SpeI (Fermentas, FastDigest) at 37 °C for 2 h.

Vector Digestion Mix:

2 µl	10 x Buffer FastDigest
10 µl	Plasmid Prep 200 ng/µl
1 µl	FastDigest ApaI
1 µl	FastDigest SpeI
6 µl	H_2O

After 2h, any undigested vector was cleaved by EcoRV (Fermentas, FastDigest) at 37 °C for 1h.

1 µl	FastDigest EcoRV

The digestion mix was separated on an agarose gel (1 %), the cleaved product was purified using the innuPrep gel extraction kit (Analytik Jena) and eluted in 15 µl H_2O (typical concentration: 70 ng/µl).

Chewback reaction

The digested and purified entry vector was chewed using T4 DNA polymerase (Enzymatics).

Chewback Reaction Mix:

10 µl	10 x NEB2
10 µl	Vector 70 ng/µl
1 µl	BSA 10 mg/ml
1 µl	dTTP 100 mM
74.66 µl	H_2O
3.33 µl	T4 DNA polymerase 3 U/µl

The reaction was incubated at 27 °C for 5 min, put on ice and subsequently inactivated at 75°C for 20min. Next, the chewed vector was diluted with the short universal reverse strand oligo (5’-PHOS-AACGGACTAGCCTTATTTTAACTTGCTATTTCTAGCTCTAAAAC-3’, PAGE purified, 100 µM, IDT) to a final buffer concentration of 2 x NEB2.

Vector Dilution Mix:

20 µl	10 x NEB2
10 µl	chewed Vector
0.5 µl	short universal reverse strand oligo 100 µM
69.5 µl	H_2O

Assembly

Gene specific sgRNA oligos (desalted, 100 µM, IDT) were diluted 1:400 in H_2O and next mixed with the Vector dilution and annealed in a PCR cycler (C100, Biorad).

Assembly Mix:

2.5 µL	Vector Dilution Mix
2.5 µL	sgRNA oligo Dilution 0.25 µM

Annealing Program:

Temp	Time	Ramp	
75 °C	2.5 min	0.1 °C/sec	│15 cycles; -1 °C per cycle
60 °C	30 min	0.1 °C/sec	
60 °C	2.5 min	0.1 °C/sec	│35 cycles; -1 °C per cycle
25 °C	∞		

Supplementary Table S1 | 96 individual sgRNA oligonucleotides

Gene	**Target site + PAM (5' -> 3')**	**Species**	**Oligo (5' -> 3')**
AIM2	GCTTTTGGCAAAACGTCTTCAGG	human	GGAAAGGACGAAACACCGCTTTTGGCAAAACGTCTTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	GGTTTTAAACACCAGCTTGAAGG	human	GGAAAGGACGAAACACCGGTTTTAAACACCAGCTTGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TTTTAAATCGTTGCTCAGTAAGG	human	GGAAAGGACGAAACACCGTTTAAATCGTTGCTCAGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TCAGCCAGGTCTTCAAGCGTTGG	human	GGAAAGGACGAAACACCGCAGCCAGGTCTTCAAGCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TTCCTCTTTCTTGATAGGGCTGG	human	GGAAAGGACGAAACACCGTCCTCTTTCTTGATAGGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	CAAAGGGAGTAAGGTGTCCGAGG	human	GGAAAGGACGAAACACCGAAAGGGAGTAAGGTGTCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	GCCAGCACGTCCACAGCCATGGG	human	GGAAAGGACGAAACACCGCCAGCACGTCCACAGCCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTTTAAATCGTTACTCAGTAAGG	human	GGAAAGGACGAAACACCGTTTAAATCGTTACTCAGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTCTATTAGTTTGCCCAAACCGG	human	GGAAAGGACGAAACACCGTCTATTAGTTTGCCCAAACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTAGCTGTGAGACGGTTGCTTGG	human	GGAAAGGACGAAACACCGTAGCTGTGAGACGGTTGCTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	ACTGGCAGTTGCGTGACGGTTGG	human	GGAAAGGACGAAACACCGCTGGCAGTTGCGTGACGGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	GGAGTAAACGAAGTGTTGGATGG	human	GGAAAGGACGAAACACCGGAGTAAACGAAGTGTTGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	TTCTATTAGTTTGTCTAGACAGG	human	GGAAAGGACGAAACACCGTCTATTAGTTTGTCTAGACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	CAAGAGCAGAGTAAGCCCCCAGG	human	GGAAAGGACGAAACACCGAAGAGCAGAGTAAGCCCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	ACTGTCACTGGGTCGTTTTGGGG	human	GGAAAGGACGAAACACCGCTGTCACTGGGTCGTTTTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	CCACTGTCACTGGGTCGTTTTGG	human	GGAAAGGACGAAACACCGCACTGTCACTGGGTCGTTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	GCGGGCCGACCGCATTTGGGAGG	human	GGAAAGGACGAAACACCGCGGGCCGACCGCATTTGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	GGCTCACTGCACCCCGTAGCAGG	human	GGAAAGGACGAAACACCGGCTCACTGCACCCCGTAGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	TCCATCCATCCCGTGTCCCAGGG	human	GGAAAGGACGAAACACCGCCATCCATCCCGTGTCCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	AGAGCACACTCTCCGGTACCTGG	human	GGAAAGGACGAAACACCGGAGCACACTCTCCGGTACCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	CAACAGGGCCCCACGGCGGAGGG	human	GGAAAGGACGAAACACCGAACAGGGCCCCACGGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	TACTCCCTCCCAAATGCGGTCGG	human	GGAAAGGACGAAACACCGACTCCCTCCCAAATGCGGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGCGCCCCTGGCATTCCGTGCGG	human	GGAAAGGACGAAACACCGGCGCCCCTGGCATTCCGTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGAGACTCGGTGGGATCCATCGG	human	GGAAAGGACGAAACACCGGAGACTCGGTGGGATCCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GAACTTTCCCGCCTTAGGCAGGG	human	GGAAAGGACGAAACACCGAACTTTCCCGCCTTAGGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGCCGCCCGTCCGCGCAACTGGG	human	GGAAAGGACGAAACACCGGCCGCCCGTCCGCGCAACTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GCCCCAGTTGCGCGGACGGGCGG	human	GGAAAGGACGAAACACCGCCCCAGTTGCGCGGACGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GCGGGCCCCAGTTGCGCGGACGG	human	GGAAAGGACGAAACACCGCGGGCCCCAGTTGCGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	AAATCCCTTCCGCTATAGAATGG	human	GGAAAGGACGAAACACCGAATCCCTTCCGCTATAGAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	ACACTCCATTCTATAGCGGAAGG	human	GGAAAGGACGAAACACCGCACTCCATTCTATAGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	CATACCCAGCGCTGGATTCAGGG	human	GGAAAGGACGAAACACCGATACCCAGCGCTGGATTCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	ATCTCTGCCTATCGCCTGGATGG	human	GGAAAGGACGAAACACCGTCTCTGCCTATCGCCTGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	TTTAAAGCCATCCAGGCGATAGG	human	GGAAAGGACGAAACACCGTTAAAGCCATCCAGGCGATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

IFIT2	GGGTGGACACGGTTAAAGTGTGG	human	GGAAAGGACGAAACACCGGGTGGACACGGTTAAAGTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	GGGTCAATGGCGTTCTGAGATGG	human	GGAAAGGACGAAACACCGGGTCAATGGCGTTCTGAGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	AGCCACAATGTGCAACCTACTGG	human	GGAAAGGACGAAACACCGGCCACAATGTGCAACCTACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	CAGCTTTACGTAAGCATTCCAGG	human	GGAAAGGACGAAACACCGAGCTTTACGTAAGCATTCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	ACTCTCAATTCTATAGGGACTGG	human	GGAAAGGACGAAACACCGCTCTCAATTCTATAGGGACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	AAACCAAAATGAAAGAGCGAAGG	human	GGAAAGGACGAAACACCGAACCAAAATGAAAGAGCGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	GGCAATTGCGATGTACCATCTGG	human	GGAAAGGACGAAACACCGGCAATTGCGATGTACCATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	CAGCTTGCCGTAAGCATTCCAGG	human	GGAAAGGACGAAACACCGAGCTTGCCGTAAGCATTCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	ACCTTGACGTATTGGTTATCAGG	human	GGAAAGGACGAAACACCGCCTTGACGTATTGGTTATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	CCAAGAGAACCTTGACGTATTGG	human	GGAAAGGACGAAACACCGCAAGAGAACCTTGACGTATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT5	CAAAGAAGAAGTACGAAGCCTGG	human	GGAAAGGACGAAACACCGAAAGAAGAAGTACGAAGCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT5	ACCTTAATATAGCTGTTATCTGG	human	GGAAAGGACGAAACACCGCCTTAATATAGCTGTTATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GCTAATGATCGACTTCAATGGGG	human	GGAAAGGACGAAACACCGCTAATGATCGACTTCAATGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GATCGCAGCGAAGATCCACACGG	human	GGAAAGGACGAAACACCGATCGCAGCGAAGATCCACAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GTCGTGTGTAGCGTTTGTTGAGG	human	GGAAAGGACGAAACACCGTCGTGTGTAGCGTTTGTTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GATGATGTTGGACTGGGCGTCGG	human	GGAAAGGACGAAACACCGATGATGTTGGACTGGGCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GCTGGACCATCCTCGGCATGTGG	human	GGAAAGGACGAAACACCGCTGGACCATCCTCGGCATGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GGATCTCCACATGCCGAGGATGG	human	GGAAAGGACGAAACACCGGATCTCCACATGCCGAGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCGCGCGCGCGACGCCATCCTGG	human	GGAAAGGACGAAACACCGCGCGCGCGCGACGCCATCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCTGGAGAACCTGACCGCCGAGG	human	GGAAAGGACGAAACACCGCTGGAGAACCTGACCGCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GGTGAGGTCCAAGGCGTCCATGG	human	GGAAAGGACGAAACACCGGTGAGGTCCAAGGCGTCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCTAACGTGCTGCGCGACATGGG	human	GGAAAGGACGAAACACCGCTAACGTGCTGCGCGACATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	CGACGCCATCCTGGATGCGCTGG	human	GGAAAGGACGAAACACCGGACGCCATCCTGGATGCGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	TCTTGAGCTCCTCGGCGGTCAGG	human	GGAAAGGACGAAACACCGCTTGAGCTCCTCGGCGGTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP4	GCTCATCCGAATATGGAGGCTGG	human	GGAAAGGACGAAACACCGCTCATCCGAATATGGAGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	GGGGCTCACTATGACATCGTGGG	human	GGAAAGGACGAAACACCGGGGCTCACTATGACATCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	TTGATCCGTATTAGGTACTAGGG	human	GGAAAGGACGAAACACCGTGATCCGTATTAGGTACTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	CTCTTTGCGAAAGAATCGCGTGG	human	GGAAAGGACGAAACACCGTCTTTGCGAAAGAATCGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	TGGGGCTCACTATGACATCGTGG	human	GGAAAGGACGAAACACCGGGGGCTCACTATGACATCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
UNC93B1	GACCTGCTCGGGGTCCCGGACGG	human	GGAAAGGACGAAACACCGACCTGCTCGGGGTCCCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
UNC93B1	GCACGTTCTTGAGCACGCCCAGG	human	GGAAAGGACGAAACACCGCACGTTCTTGAGCACGCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
UNC93B1	GCTCACCTACGGCGTCTACCTGG	human	GGAAAGGACGAAACACCGCTCACCTACGGCGTCTACCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	ATGGGTGACTGGAGCGCCTTAGG	human	GGAAAGGACGAAACACCGTGGGTGACTGGAGCGCCTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	TGAGCCAGGTACAAGAGTGTGGG	human	GGAAAGGACGAAACACCGGAGCCAGGTACAAGAGTGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	ATGGTAAGGTGAAAATGCGAGGG	human	GGAAAGGACGAAACACCGTGGTAAGGTGAAAATGCGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

GJC1	GAACACCCAGAAGCGTACATGGG	human	GGAAAGGACGAAACACCGAACACCCAGAAGCGTACATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJC1	GCAAGCCCTATGCAATGCGCTGG	human	GGAAAGGACGAAACACCGCAAGCCCTATGCAATGCGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJC1	CTTCCTGACTCGCCTGCTAGAGG	human	GGAAAGGACGAAACACCGTTCCTGACTCGCCTGCTAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	TAACGGAGTCAATCAAAGCTCGG	human	GGAAAGGACGAAACACCGAACGGAGTCAATCAAAGCTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	ATTGACTCCGTTATTCCGAAAGG	human	GGAAAGGACGAAACACCGTTGACTCCGTTATTCCGAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	TGACTCCGTTATTCCGAAAGGGG	human	GGAAAGGACGAAACACCGGACTCCGTTATTCCGAAAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	CTGTGCCCCTTTCGGAATAACGG	human	GGAAAGGACGAAACACCGTGTGCCCCTTTCGGAATAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
AAVS1	GGGGCCACTAGGGACAGGATTGG	human	GGAAAGGACGAAACACCGGGGCCACTAGGGACAGGATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTGCCCAAACCGGCATCACCTGG	human	GGAAAGGACGAAACACCGTGCCCAAACCGGCATCACCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	GCAAAGAGTCTACCAAGATCAGG	human	GGAAAGGACGAAACACCGCAAAGAGTCTACCAAGATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT5	GAAGAAGCTCAGAAGTATACAGG	human	GGAAAGGACGAAACACCGAAGAAGCTCAGAAGTATACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GGCGCCGTCGTCCTTCTACGCGG	mouse	GGAAAGGACGAAACACCGGCGCCGTCGTCCTTCTACGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GCGGACGGCTTCTTAGCGCGTGG	mouse	GGAAAGGACGAAACACCGCGGACGGCTTCTTAGCGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GTCGGGGCGCGCTTCGCGGACGG	mouse	GGAAAGGACGAAACACCGTCGGGGCGCGCTTCGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GCAGCTTTCCGCGTGGGCCCTGG	mouse	GGAAAGGACGAAACACCGCAGCTTTCCGCGTGGGCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GCGGGCCGCAGCTTTCCGCGTGG	mouse	GGAAAGGACGAAACACCGCGGGCCGCAGCTTTCCGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GAAAGCTGCGGCCCGCAAAGGGG	mouse	GGAAAGGACGAAACACCGAAAGCTGCGGCCCGCAAAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GGGGGCTCGATCGCGGCGGGCGG	mouse	GGAAAGGACGAAACACCGGGGGCTCGATCGCGGCGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GGTGGCTCCTGCCGCGTCCATGG	mouse	GGAAAGGACGAAACACCGGTGGCTCCTGCCGCGTCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
Mb21d1	GGCTGGGGCTCCCGTACGGCGGG	mouse	GGAAAGGACGAAACACCGGCTGGGGCTCCCGTACGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 16	-	Random	GGAAAGGACGAAACACCGACTGAGAACCCGAAAACAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 26	-	Random	GGAAAGGACGAAACACCGACTTCGTTTACTCCGAATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 72	-	Random	GGAAAGGACGAAACACCGAAAAAAGCTCATCCGAATAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 73	-	Random	GGAAAGGACGAAACACCGAGCGCTGACTCCATATCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 78	-	Random	GGAAAGGACGAAACACCGAAACCTCTTCTGCAAATCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 81	-	Random	GGAAAGGACGAAACACCGCCCACCAGCTCGTCCAGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 82	-	Random	GGAAAGGACGAAACACCGCGCCCACCAGCTCGTCCAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
gRNA 85	-	Random	GGAAAGGACGAAACACCGAGGCCCAGGTAGACGCCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

Supplementary Table S2 | Genome editing activities of 71 CRISPR constructs

Gene	Target site + PAM (5' -> 3')	Background Activity [%]	Activity N1 [%]	Activity N2 [%]	Oligo (5' -> 3')
CASP1	ATTGACTCCGTTATTCCGAAAGG	0,02	62,65	34,41	GGAAAGGACGAAACACCGTTGACTCCGTTATTCCGAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	CTGTGCCCCTTTCGGAATAACGG	0,09	49,16	25,96	GGAAAGGACGAAACACCGTGTGCCCCTTTCGGAATAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	TAACGGAGTCAATCAAAGCTCGG	0,09	35,61	25,49	GGAAAGGACGAAACACCGAACGGAGTCAATCAAAGCTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP1	TGACTCCGTTATTCCGAAAGGGG	0,06	62,71	49,15	GGAAAGGACGAAACACCGGACTCCGTTATTCCGAAAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP4	GCTCATCCGAATATGGAGGCTGG	0,00	63,17	79,84	GGAAAGGACGAAACACCGCTCATCCGAATATGGAGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	CTCTTTGCGAAAGAATCGCGTGG	0,02	76,72	72,74	GGAAAGGACGAAACACCGTCTTTGCGAAAGAATCGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	GGGGCTCACTATGACATCGTGGG	0,00	66,19	44,68	GGAAAGGACGAAACACCGGGGCTCACTATGACATCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	TGGGGCTCACTATGACATCGTGG	0,00	85,65	44,03	GGAAAGGACGAAACACCGGGGGCTCACTATGACATCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CASP5	TTGATCCGTATTAGGTACTAGGG	0,03	71,06	53,64	GGAAAGGACGAAACACCGTGATCCGTATTAGGTACTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	ATGGGTGACTGGAGCGCCTTAGG	0,04	68,52	63,00	GGAAAGGACGAAACACCGTGGGTGACTGGAGCGCCTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	ATGGTAAGGTGAAAATGCGAGGG	0,09	95,69	51,64	GGAAAGGACGAAACACCGTGGTAAGGTGAAAATGCGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJA1	TGAGCCAGGTACAAGAGTGTGGG	0,01	87,26	50,26	GGAAAGGACGAAACACCGGAGCCAGGTACAAGAGTGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJC1	CTTCCTGACTCGCCTGCTAGAGG	0,02	74,96	97,63	GGAAAGGACGAAACACCGTTCCTGACTCGCCTGCTAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJC1	GAACACCCAGAAGCGTACATGGG	0,01	89,79	48,92	GGAAAGGACGAAACACCGAACACCCAGAAGCGTACATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GJC1	GCAAGCCCTATGCAATGCGCTGG	0,00	71,32	56,25	GGAAAGGACGAAACACCGCAAGCCCTATGCAATGCGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	CAAAGGGAGTAAGGTGTCCGAGG	0,00	84,15	74,55	GGAAAGGACGAAACACCGAAAGGGAGTAAGGTGTCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	GGTTTTAAACACCAGCTTGAAGG	0,03	37,19	17,15	GGAAAGGACGAAACACCGGTTTTAAACACCAGCTTGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TCAGCCAGGTCTTCAAGCGTTGG	0,05	90,30	56,78	GGAAAGGACGAAACACCGCAGCCAGGTCTTCAAGCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TTCCTCTTTCTTGATAGGGCTGG	0,03	54,95	33,23	GGAAAGGACGAAACACCGTCCTCTTTCTTGATAGGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFI16	TTTTAAATCGTTGCTCAGTAAGG	0,00	0,21	0,05	GGAAAGGACGAAACACCGTTTAAATCGTTGCTCAGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	AAATCCCTTCCGCTATAGAATGG	0,72	72,20	78,79	GGAAAGGACGAAACACCGAATCCCTTCCGCTATAGAAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	ACACTCCATTCTATAGCGGAAGG	0,04	79,08	47,76	GGAAAGGACGAAACACCGCACTCCATTCTATAGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	ATCTCTGCCTATCGCCTGGATGG	5,88	64,16	51,66	GGAAAGGACGAAACACCGTCTCTGCCTATCGCCTGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	CATACCCAGCGCTGGATTCAGGG	0,05	66,76	55,20	GGAAAGGACGAAACACCGATACCCAGCGCTGGATTCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT1	TTTAAAGCCATCCAGGCGATAGG	0,00	80,90	54,93	GGAAAGGACGAAACACCGTTAAAGCCATCCAGGCGATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	AAACCAAAATGAAAGAGCGAAGG	0,00	74,04	79,68	GGAAAGGACGAAACACCGAACCAAAATGAAAGAGCGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	ACTCTCAATTCTATAGGGACTGG	0,13	78,45	79,02	GGAAAGGACGAAACACCGCTCTCAATTCTATAGGGACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	AGCCACAATGTGCAACCTACTGG	0,00	69,58	57,35	GGAAAGGACGAAACACCGGCCACAATGTGCAACCTACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	CAGCTTTACGTAAGCATTCCAGG	0,00	19,88	27,44	GGAAAGGACGAAACACCGAGCTTTACGTAAGCATTCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	GGGTCAATGGCGTTCTGAGATGG	0,01	83,22	76,34	GGAAAGGACGAAACACCGGGTCAATGGCGTTCTGAGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT2	GGGTGGACACGGTTAAAGTGTGG	0,00	79,44	75,16	GGAAAGGACGAAACACCGGGTGGACACGGTTAAAGTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	ACCTTGACGTATTGGTTATCAGG	0,03	37,91	57,11	GGAAAGGACGAAACACCGCCTTGACGTATTGGTTATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	CAGCTTGCCGTAAGCATTCCAGG	0,01	49,37	40,27	GGAAAGGACGAAACACCGAGCTTGCCGTAAGCATTCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

IFIT3	CCAAGAGAACCTTGACGTATTGG	0,00	54,24	45,26	GGAAAGGACGAAACACCGCAAGAGAACCTTGACGTATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT3	GGCAATTGCGATGTACCATCTGG	0,00	87,17	57,66	GGAAAGGACGAAACACCGGCAATTGCGATGTACCATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT5	ACCTTAATATAGCTGTTATCTGG	0,04	47,21	55,43	GGAAAGGACGAAACACCGCCTTAATATAGCTGTTATCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIT5	CAAAGAAGAAGTACGAAGCCTGG	0,01	65,67	47,57	GGAAAGGACGAAACACCGAAAGAAGAAGTACGAAGCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GAACTTTCCCGCCTTAGGCAGGG	0,00	72,06	44,76	GGAAAGGACGAAACACCGAACTTTCCCGCCTTAGGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GCGGGCCCCAGTTGCGCGGACGG	0,07	47,72	28,55	GGAAAGGACGAAACACCGCCCCAGTTGCGCGGACGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGAGACTCGGTGGGATCCATCGG	0,00	34,89	40,15	GGAAAGGACGAAACACCGGAGACTCGGTGGGATCCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGCCGCCCGTCCGCGCAACTGGG	0,02	25,59	33,00	GGAAAGGACGAAACACCGGCCGCCCGTCCGCGCAACTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MB21D1	GGCGCCCCTGGCATTCCGTGCGG	0,04	68,47	50,99	GGAAAGGACGAAACACCGGCGCCCCTGGCATTCCGTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	CAAGAGCAGAGTAAGCCCCCAGG	0,08	69,13	63,53	GGAAAGGACGAAACACCGAAGAGCAGAGTAAGCCCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	CCACTGTCACTGGGTCGTTTTGG	0,08	47,95	45,45	GGAAAGGACGAAACACCGCACTGTCACTGGGTCGTTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	GGAGTAAACGAAGTGTTGGATGG	0,01	56,49	57,03	GGAAAGGACGAAACACCGGAGTAAACGAAGTGTTGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MNDA	TTCTATTAGTTTGTCTAGACAGG	0,01	6,28	1,26	GGAAAGGACGAAACACCGTCTATTAGTTTGTCTAGACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GATCGCAGCGAAGATCCACACGG	0,02	74,21	63,60	GGAAAGGACGAAACACCGATCGCAGCGAAGATCCACAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GATGATGTTGGACTGGGCGTCGG	0,02	85,00	60,68	GGAAAGGACGAAACACCGATGATGTTGGACTGGGCGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GCTAATGATCGACTTCAATGGGG	0,00	76,49	66,03	GGAAAGGACGAAACACCGCTAATGATCGACTTCAATGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GCTGGACCATCCTCGGCATGTGG	0,00	57,78	58,11	GGAAAGGACGAAACACCGCTGGACCATCCTCGGCATGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GGATCTCCACATGCCGAGGATGG	0,01	63,58	59,67	GGAAAGGACGAAACACCGGATCTCCACATGCCGAGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NLRP3	GTCGTGTGTAGCGTTTGTTGAGG	0,10	74,03	57,88	GGAAAGGACGAAACACCGTCGTGTGTAGCGTTTGTTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	CGACGCCATCCTGGATGCGCTGG	N.D.	96,56	63,72	GGAAAGGACGAAACACCGGACGCCATCCTGGATGCGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCGCGCGCGCGACGCCATCCTGG	0,38	39,35	40,53	GGAAAGGACGAAACACCGCGCGCGCGCGACGCCATCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCTAACGTGCTGCGCGACATGGG	0,05	49,76	56,38	GGAAAGGACGAAACACCGCTAACGTGCTGCGCGACATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GCTGGAGAACCTGACCGCCGAGG	0,15	81,02	70,75	GGAAAGGACGAAACACCGCTGGAGAACCTGACCGCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	GGTGAGGTCCAAGGCGTCCATGG	0,01	82,00	70,51	GGAAAGGACGAAACACCGGTGAGGTCCAAGGCGTCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYCARD	TCTTGAGCTCCTCGGCGGTCAGG	0,03	30,79	23,91	GGAAAGGACGAAACACCGCTTGAGCTCCTCGGCGGTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	ACTGGCAGTTGCGTGACGGTTGG	0,02	53,79	37,39	GGAAAGGACGAAACACCGCTGGCAGTTGCGTGACGGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	GCCAGCACGTCCACAGCCATGGG	0,00	49,92	88,56	GGAAAGGACGAAACACCGCCAGCACGTCCACAGCCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTAGCTGTGAGACGGTTGCTTGG	0,03	65,31	52,00	GGAAAGGACGAAACACCGTAGCTGTGAGACGGTTGCTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTCTATTAGTTTGCCCAAACCGG	0,06	21,58	10,91	GGAAAGGACGAAACACCGTCTATTAGTTTGCCCAAACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PYHIN1	TTTTAAATCGTTACTCAGTAAGG	0,01	0,38	0,04	GGAAAGGACGAAACACCGTTTAAATCGTTACTCAGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	AGAGCACACTCTCCGGTACCTGG	0,00	63,20	61,59	GGAAAGGACGAAACACCGGAGCACACTCTCCGGTACCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	CAACAGGGCCCCACGGCGGAGGG	0,05	16,55	0,37	GGAAAGGACGAAACACCGAACAGGGCCCCACGGCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	GCGGGCCGACCGCATTTGGGAGG	0,00	74,43	59,19	GGAAAGGACGAAACACCGCGGGCCGACCGCATTTGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	GGCTCACTGCACCCCGTAGCAGG	0,00	75,86	43,58	GGAAAGGACGAAACACCGGCTCACTGCACCCCGTAGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TMEM173	TACTCCCTCCCAAATGCGGTCGG	0,20	73,05	45,63	GGAAAGGACGAAACACCGACTCCCTCCCAAATGCGGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

TMEM173	TCCATCCATCCCGTGTCCCAGGG	0,03	79,71	50,93	GGAAAGGACGAAACACCGCCATCCATCCCGTGTCCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
UNC93B1	GCACGTTCTTGAGCACGCCCAGG	0,00	87,50	86,35	GGAAAGGACGAAACACCGCACGTTCTTGAGCACGCCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
UNC93B1	GCTCACCTACGGCGTCTACCTGG	0,00	64,09	70,99	GGAAAGGACGAAACACCGCTCACCTACGGCGTCTACCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

Supplementary Table S5 | Genome editing activity of 43 CRISPR constructs from genome wide library

Gene	Target site + PAM (5' -> 3')	Background Activity [%]	Activity [%]	Oligo (5' -> 3')
AGXT	GTGGACATCGGGGAGCGCATAGG	0,01	64,37	GGAAAGGACGAAACACCGTGGACATCGGGGAGCGCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
AIFM1	CCGTGTGCGTCCGAAGCCCGAGG	0,00	68,03	GGAAAGGACGAAACACCGCGTGTGCGTCCGAAGCCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ARG1	AGGAGCTCCAATAATCCCTATGG	0,04	74,63	GGAAAGGACGAAACACCGGGAGCTCCAATAATCCCTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ARG2	GGATGGAATGCACTCGCGTCTGG	0,00	54,29	GGAAAGGACGAAACACCGGATGGAATGCACTCGCGTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ASL	GAGCTCATTGGTGCAACGGCAGG	0,03	55,62	GGAAAGGACGAAACACCGAGCTCATTGGTGCAACGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ATF3	GGCAGAAGCACTCACTTCCGAGG	0,01	72,07	GGAAAGGACGAAACACCGGCAGAAGCACTCACTTCCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CTSB	GCCTGCAAGCTTCGATGCACGGG	0,00	68,17	GGAAAGGACGAAACACCGCCTGCAAGCTTCGATGCACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CYBB	GTAAGACCTCCGGATGGTTTTGG	0,00	39,34	GGAAAGGACGAAACACCGTAAGACCTCCGGATGGTTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
DDX58	GGGTCTTCCGGATATAATCCTGG	0,05	75,93	GGAAAGGACGAAACACCGGGTCTTCCGGATATAATCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
DES	GCTGGCTGGACGAGTAGGCCTGG	0,00	85,45	GGAAAGGACGAAACACCGCTGGCTGGACGAGTAGGCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ERBB2	GGTGGGTCTCGGGACTGGCAGGG	0,02	53,67	GGAAAGGACGAAACACCGGTGGGTCTCGGGACTGGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
ERBB3	CAGCATCGCCGGTCACACTCAGG	0,00	64,86	GGAAAGGACGAAACACCGAGCATCGCCGGTCACACTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
GGCX	GCTGCTGGCCAGCATGACGTAGG	0,03	66,73	GGAAAGGACGAAACACCGCTGCTGGCCAGCATGACGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IFIH1	GAGGGCTGCCGGTTCTCCGGAGG	0,03	67,69	GGAAAGGACGAAACACCGAGGGCTGCCGGTTCTCCGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
CHUK	TAGTTTAGTAGTAGAACCCATGG	0,02	69,89	GGAAAGGACGAAACACCGAGTTTAGTAGTAGAACCCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IKBKG	AATCTGGTTGCTCTGCCGGATGG	0,01	47,79	GGAAAGGACGAAACACCGATCTGGTTGCTCTGCCGGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IRAK4	GATGAACGACCCATTTCTGTTGG	0,02	65,24	GGAAAGGACGAAACACCGATGAACGACCCATTTCTGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IRF1	GGCCCAGCTCCGGAACAAACAGG	0,02	54,56	GGAAAGGACGAAACACCGGCCCAGCTCCGGAACAAACGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IRF3	GGAGGATTTCGGAATCTTCCAGG	0,00	5,28	GGAAAGGACGAAACACCGGAGGATTTCGGAATCTTCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IRF5	GGGCTTCAGCCGCACGCGGCGGG	0,00	24,17	GGAAAGGACGAAACACCGGGCTTCAGCCGCACGCGGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
IRF7	GCAGCCCCACGCGTGCTGTTCGG	0,03	49,20	GGAAAGGACGAAACACCGCAGCCCCACGCGTGCTGTTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
KDR	GGTAACCAAGGTACTTCGCAGGG	0,05	67,69	GGAAAGGACGAAACACCGGTAACCAAGGTACTTCGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MAP3K7	GTAAACACCAACTCATTGCGTGG	N.D.	65,96	GGAAAGGACGAAACACCGTAAACACCAACTCATTGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
MAVS	TACTTCATTGCGGCACTGAGGGG	N.D.	41,12	GGAAAGGACGAAACACCGACTTCATTGCGGCACTGAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NAP1	GGCCTATCATGCATATCGAGAGG	0,00	63,49	GGAAAGGACGAAACACCGGCCTATCATGCATATCGAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NCBP2	CGTCCCATTTATGTACCGCATGG	0,04	40,42	GGAAAGGACGAAACACCGGTCCCATTTATGTACCGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
NCF1	CCACCTCCTCGACTTCTTCAAGG	0,04	14,80	GGAAAGGACGAAACACCGCACCTCCTCGACTTCTTCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
OASL	GGGCTCCTTCGGGAATGGCACGG	0,29	45,95	GGAAAGGACGAAACACCGGGCTCCTTCGGGAATGGCAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
OTC	GAATGAAAGTCTCACGGACACGG	N.D.	52,14	GGAAAGGACGAAACACCGAATGAAAGTCTCACGGACAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
PSPH	CCTACAGGAGCGAAATGTTCAGG	0,00	40,61	GGAAAGGACGAAACACCGCTACAGGAGCGAAATGTTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
RIPK1	GCTCCTGGGCGTCATCATAGAGG	7,58	42,83	GGAAAGGACGAAACACCGCTCCTGGGCGTCATCATAGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

SOLH	GTTGAGGTCGGGCTTGTGCCGGG	0,05	48,85	GGAAAGGACGAAACACCGTTGAGGTCGGGCTTGTGCCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TANK	CTCTGTGCCTATACAGTGTACGG	0,02	21,20	GGAAAGGACGAAACACCGTCTGTGCCTATACAGTGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TBK1	TTCAGATTCTGGTAGTCCATAGG	0,00	82,59	GGAAAGGACGAAACACCGTCAGATTCTGGTAGTCCATGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TP53	GAGCGCTGCTCAGATAGCGATGG	0,02	64,19	GGAAAGGACGAAACACCGAGCGCTGCTCAGATAGCGAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRAF4	GTGGTGCCCGCATGATGCGGCGG	0,02	56,04	GGAAAGGACGAAACACCGTGGTGCCCGCATGATGCGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRAF5	CAAACGCATGTGCTCCCGTAAGG	0,01	46,28	GGAAAGGACGAAACACCGAAACGCATGTGCTCCCGTAGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRAF7	GCTACAACCGCTTCTCCGGGGGG	0,12	50,79	GGAAAGGACGAAACACCGCTACAACCGCTTCTCCGGGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRIM13	GGAGTGTGCGGAATTCCTTGTGG	0,01	73,04	GGAAAGGACGAAACACCGGAGTGTGCGGAATTCCTTGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRIM25	GTCGCGCCTGGTAGACGGCGCGG	0,00	1,80	GGAAAGGACGAAACACCGTCGCGCCTGGTAGACGGCGGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
TRIM68	CCAGCTGCCAATTAGGCCGCAGG	0,00	30,07	GGAAAGGACGAAACACCGCAGCTGCCAATTAGGCCGCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
VEZT	ACCACCTCTTCGTCAAACTCCGG	0,05	64,71	GGAAAGGACGAAACACCGCCACCTCTTCGTCAAACTCGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG
VKORC1L1	CTTCTCCCGCTCCACGTGGTAGG	0,00	43,62	GGAAAGGACGAAACACCGTTCTCCCGCTCCACGTGGTGTTTTAGAGCTAGAAATAGCAAGTTAAAATAAGG

Supplementary Table S6 | Primer sequences

Primers for amplifying gRNA sequences from orthogonal pools (first PCR):

grna fwd 1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATTACTCGCTCGGTGCCACTTTTTCAAGTTG
grna fwd 2	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCGGAGACTCGGTGCCACTTTTTCAAGTTG
grna fwd 3	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCGCTCATTCTCGGTGCCACTTTTTCAAGTTG
grna fwd 4	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAGATTCCCTCGGTGCCACTTTTTCAAGTTG
grna fwd 5	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATTCAGAACTCGGTGCCACTTTTTCAAGTTG
grna fwd 6	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAATTCGTCTCGGTGCCACTTTTTCAAGTTG
grna fwd 7	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTGAAGCTCTCGGTGCCACTTTTTCAAGTTG
grna fwd 8	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTAATGCGCCTCGGTGCCACTTTTTCAAGTTG
grna fwd 9	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCGGCTATGCTCGGTGCCACTTTTTCAAGTTG
grna fwd 10	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCGCGAACTCGGTGCCACTTTTTCAAGTTG
grna fwd 11	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTCGCGCCTCGGTGCCACTTTTTCAAGTTG
grna fwd 12	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGCGATAGCTCGGTGCCACTTTTTCAAGTTG
grna rev	TGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTACGATACAAGGCTGTTAGAGAG

Illumina barcoding primers (second PCR):

Illu fwd 1	AATGATACGGCGACCACCGAGATCTACAC**TATAGCCT**ACACTCTTTCCCTACACGACGCT
Illu fwd 2	AATGATACGGCGACCACCGAGATCTACAC**ATAGAGGC**ACACTCTTTCCCTACACGACGCT
Illu fwd 3	AATGATACGGCGACCACCGAGATCTACAC**CCTATCCT**ACACTCTTTCCCTACACGACGCT
Illu fwd 4	AATGATACGGCGACCACCGAGATCTACAC**GGCTCTGA**ACACTCTTTCCCTACACGACGCT
Illu fwd 5	AATGATACGGCGACCACCGAGATCTACAC**AGGCGAAG**ACACTCTTTCCCTACACGACGCT
Illu fwd 6	AATGATACGGCGACCACCGAGATCTACAC**TAATCTTA**ACACTCTTTCCCTACACGACGCT
Illu fwd 7	AATGATACGGCGACCACCGAGATCTACAC**CAGGACGT**ACACTCTTTCCCTACACGACGCT
Illu fwd 8	AATGATACGGCGACCACCGAGATCTACAC**GTACTGAC**ACACTCTTTCCCTACACGACGCT
Illu fwd 9	AATGATACGGCGACCACCGAGATCTACAC**GCGAAGAT**ACACTCTTTCCCTACACGACGCT
Illu fwd 10	AATGATACGGCGACCACCGAGATCTACAC**CCCTTGTG**ACACTCTTTCCCTACACGACGCT
Illu fwd 11	AATGATACGGCGACCACCGAGATCTACAC**TCGCATCA**ACACTCTTTCCCTACACGACGCT
Illu fwd 12	AATGATACGGCGACCACCGAGATCTACAC**AGAATCAA**ACACTCTTTCCCTACACGACGCT
Illu fwd 13	AATGATACGGCGACCACCGAGATCTACAC**GTTTGAGC**ACACTCTTTCCCTACACGACGCT
Illu fwd 14	AATGATACGGCGACCACCGAGATCTACAC**GACTAACG**ACACTCTTTCCCTACACGACGCT
Illu fwd 15	AATGATACGGCGACCACCGAGATCTACAC**CTCACATA**ACACTCTTTCCCTACACGACGCT
Illu fwd 16	AATGATACGGCGACCACCGAGATCTACAC**CCTGAAAC**ACACTCTTTCCCTACACGACGCT

Illu rev 1	CAAGCAGAAGACGGCATACGAGAT**CGAGTAAT**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 2	CAAGCAGAAGACGGCATACGAGAT**TCTCCGGA**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 3	CAAGCAGAAGACGGCATACGAGAT**AATGAGCG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 4	CAAGCAGAAGACGGCATACGAGAT**GGAATCTC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 5	CAAGCAGAAGACGGCATACGAGAT**TTCTGAAT**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 6	CAAGCAGAAGACGGCATACGAGAT**ACGAATTC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 7	CAAGCAGAAGACGGCATACGAGAT**AGCTTCAG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 8	CAAGCAGAAGACGGCATACGAGAT**GCGCATTA**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 9	CAAGCAGAAGACGGCATACGAGAT**CATAGCCG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 10	CAAGCAGAAGACGGCATACGAGAT**TTCGCGGA**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 11	CAAGCAGAAGACGGCATACGAGAT**GCGCGAGA**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 12	CAAGCAGAAGACGGCATACGAGAT**CTATCGCT**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 13	CAAGCAGAAGACGGCATACGAGAT**TGTAGTGC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 14	CAAGCAGAAGACGGCATACGAGAT**GCGTCGAC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 15	CAAGCAGAAGACGGCATACGAGAT**GGTCTTCT**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 16	CAAGCAGAAGACGGCATACGAGAT**AAATGTCC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 17	CAAGCAGAAGACGGCATACGAGAT**GTTGAAAC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 18	CAAGCAGAAGACGGCATACGAGAT**TCTTTACG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 19	CAAGCAGAAGACGGCATACGAGAT**ATGCCTGG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 20	CAAGCAGAAGACGGCATACGAGAT**CAATAAGG**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 21	CAAGCAGAAGACGGCATACGAGAT**CGCCGTAA**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 22	CAAGCAGAAGACGGCATACGAGAT**TAAGGCTT**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 23	CAAGCAGAAGACGGCATACGAGAT**TTGCTGCC**GTGACTGGAGTTCAGACGTGTGCT
Illu rev 24	CAAGCAGAAGACGGCATACGAGAT**CTCAATGT**GTGACTGGAGTTCAGACGTGTGCT

Supplementary Table S7 | Vector sequences

pR-U6-gRNA
CTGCAGCCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGAT
GGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGAT
GGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGACCTG
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GCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTG
TATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGAT
TGACTACCCGTCAGCGGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGA
CCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGATTTTA
TGCGCCTGCGTCGGTACTAGCTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGGTGGAACTGACGAGTTC
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pL-U6-gRNA
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